

## AMENDMENTS TO THE CLAIMS

Claims 1-22 (cancelled).

23. (currently amended): ~~The pharmaceutical composition according to claim 21 wherein said peptide analogue has the A pharmaceutical composition for the gastrointestinal delivery by oral administration of an LH-RH peptide analogue, said composition comprising a therapeutically effective amount of a peptide analogue in combination with α-cyclodextrin and excipients suitable for the gastrointestinal delivery of the peptide analogue, wherein the α-cyclodextrin enhances the biological activity of of the LH-RH peptide analogue when orally administered, said LH-RH peptide analogue having the formula (SEQ ID N°: 1):~~

A1-A2-A3-A4-A5-A6-A7-A8-Pro-Z (A)

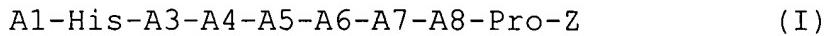
in which :

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated ;
- A2 is a direct bond ; His ; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid ; or a basic L- or D-amino acid;
- A6 is Gly ; (S)-spirolactam-Pro ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl, a (C<sub>2</sub>-C<sub>7</sub>)acyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side

chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;

- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L- or D-amino acid ;
- Z is GlyNH<sub>2</sub> ; D-AlaNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

24. (previously presented): The pharmaceutical composition according to claim 23 wherein said peptide analogue has the formula (SEQ ID N° : 2):

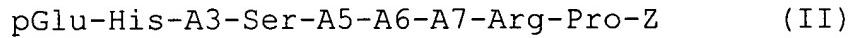


in which:

- A1 is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid ;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid ;
- A6 is Gly ; D-Pro ; (S)-spirolactam-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic D-amino acid ;

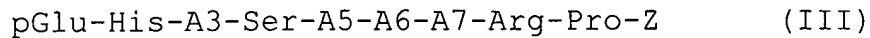
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid ;
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

25. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEQ ID N°: 3):



in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

26. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEQ ID N°: 4):



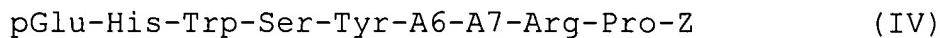
in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe ;
- A6 is (S)-spirolactam-Pro ; Gly; D-Pro ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-His or D-His(Bzl) ; D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha ; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly ; D-perhydronaphtyl-Ala ; D-perhydrodiphenyl-Ala or D-APhe

optionally substituted by an aminotriazolyl group;

- A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group;
- Z is GlyNH<sub>2</sub>, azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

27. (previously presented): The pharmaceutical composition according to claim 24 wherein said peptide analogue has the formula (SEQ ID N° :5) :

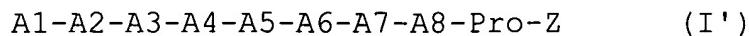


in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-Ser(OBut) or D-Trp;
- A7 is Leu, MeLeu, Npg or MeNpg;
- Z is GlyNH<sub>2</sub>, azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

28. (previously presented): The pharmaceutical composition according to claim 24 wherein the peptide analogue is selected from the group consisting of leuprorelin, [Npg<sup>7</sup>]-leuprorelin, triptorelin, [Npg<sup>7</sup>]-triptorelin, goserelin, [Npg<sup>7</sup>]-goserelin, buserelin and [Npg<sup>7</sup>]-buserelin.

29. (withdrawn): The pharmaceutical composition according to claim 23 wherein said peptide analogue has the formula (SEQ ID N°:6):



in which:

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;

- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Asn ; D-Pen ; D-(S-Me) Pen ; D-(S-Et) Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(O-Bu<sup>t</sup>) ; D-Thr(O-Bu<sup>t</sup>) ; D-Cys(O-Bu<sup>t</sup>) ; D-Ser(O-R<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.

30. (withdrawn): The pharmaceutical composition according to claim 29 wherein the peptide analogue has the formula (SEQ ID N°:7):

Ac-D-Nal-D-pClPhe-D-Pal-Ser-A5-A6-A7-A8-Pro-D-AlaNH<sub>2</sub> (II')

in which :

- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.

31. (withdrawn): The pharmaceutical composition according to claim 29 wherein the peptide analogue is selected from the group consisting of antide, [Npg<sup>7</sup>]-antide, cetrorelix, [Npg<sup>7</sup>]-

cetrorelix, abarelix and [Npg<sup>7</sup>]-abarelix.

32. (previously presented): The pharmaceutical composition according to claim 21 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxy-methylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

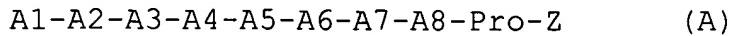
33. (previously presented): The pharmaceutical composition according to claim 32 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

34. (currently amended): The pharmaceutical composition according to claim 24 23 which further comprises a compound selected from the group consisting of a protease inhibitor, an absorption enhancer, and mixtures thereof.

35. (currently amended): A method of enhancing the biological activity of a LH-RH peptide analogue which comprises orally administering to a patient in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a peptide analogue in combination with  $\alpha$ -cyclodextrin and excipients suitable for the gastrointestinal delivery of the peptide analogue, wherein the  $\alpha$ -cyclodextrin enhances the biological activity of the LH-RH peptide analogue when orally administered a therapeutically effective amount of said analogue in combination with  $\alpha$ -cyclodextrin or a derivative thereof.

36. (previously presented): The method according to claim

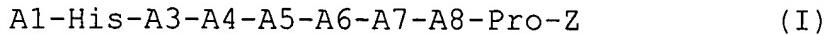
35, wherein said peptide analogue has the formula (SEQ ID N°:1) :



in which :

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond ; His ; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid ;
- A6 is Gly ; (S)-spirolactam-Pro ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Asn ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl, a (C<sub>2</sub>-C<sub>7</sub>)acyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms ;
- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> ; D-AlaNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

37. (previously presented): The method according to claim 36 wherein said peptide analogue has the formula (SEQ ID N° : 2) :

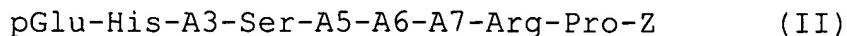


in which:

- A1 is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid ;
- A6 is Gly ; D-Pro ; (S)-spirolactam-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid;
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

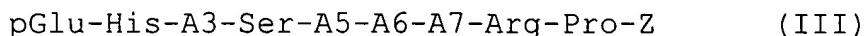
38. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID N° :

3) :



in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

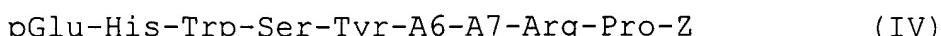
39. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID N° : 4) :



in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe ;
- A6 is (S)-spirolactam-Pro ; Gly; D-Pro ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-His or D-His(Bzl) ; D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha ; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly ; D-perhydronaphtyl-Ala ; D-perhydrodiphenyl-Ala ; or D-APhe optionally substituted by an aminotriazolyl group ;
- A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group;
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

40. (previously presented): The method according to claim 37 wherein said peptide analogue has the formula (SEQ ID N° : 5) :



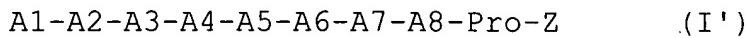
in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-Ser(OBu<sup>t</sup>) or D-Trp;
- A7 is Leu, MeLeu, Npg or MeNpg;

- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

41. (previously presented): The method according to claim 37 wherein the peptide analogue is selected from the group consisting of leuprorelin, [Npg<sup>7</sup>]-leuprorelin, triptorelin, [Npg<sup>7</sup>]-triptorelin, goserelin, [Npg<sup>7</sup>]-goserelin, buserelin and [Npg<sup>7</sup>]-buserelin.

42. (withdrawn): The method according to claim 36 wherein said peptide analogue has the formula (SEQ ID N° : 6) :



in which:

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Asn ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(O-Bu<sup>t</sup>) ; D-Thr(O-Bu<sup>t</sup>) ; D-Cys(O-Bu<sup>t</sup>) ; D-Ser(O-R<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;

- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.

43. (withdrawn): The method according to claim 42 wherein the peptide analogue has the formula (SEQ ID N° : 7):

Ac-D-Nal-D-pClPhe-D-Pal-Ser-A5-A6-A7-A8-Pro-D-AlaNH<sub>2</sub> (II')  
in which :

- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.

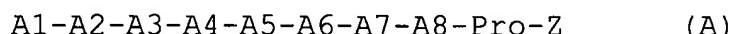
44. (withdrawn): The method according to claim 42 wherein the peptide analogue is selected from the group consisting of antide, [Npg<sup>7</sup>]-antide, cetrorelix, [Npg<sup>7</sup>]-cetrorelix, abarelix and [Npg<sup>7</sup>]-abarelix.

45. (previously presented): The method according to claim 35 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

46. (previously presented): The method according to claim 45 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

47. (previously presented): A method of treating a disease wherein a LH-RH agonist or antagonist action is required which comprises orally administering to a patient in need thereof a

therapeutically effective amount of a LH-RH peptide analogue in combination with  $\alpha$ -cyclodextrin or a derivative thereof, wherein said peptide analogue has the formula (SEQ ID N° : 1) :

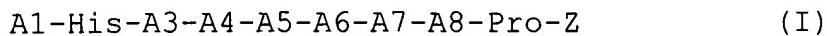


in which :

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond ; His ; or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid ;
- A6 is Gly ; (S)-spirolactam-Pro ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Asn ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl, a (C<sub>2</sub>-C<sub>7</sub>)acyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms ;
- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> ; D-AlaNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a

heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

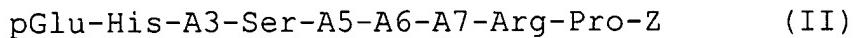
48. (previously presented): The method according to claim 47 wherein said peptide analogue has the formula (SEQ ID N°: 2):



in which:

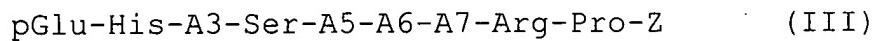
- A1 is pGlu, Sar or AcSar;
- A3 is an aromatic L-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBu<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid ;
- A6 is Gly ; D-Pro ; (S)-spirolactam-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-Ser(OR<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aza-amino acid ; D-His which may be substituted on the imidazole ring by a (C<sub>1</sub>-C<sub>6</sub>)alkyl or a benzyl group ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;
- A8 is a basic L-amino acid;
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> ; or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C<sub>1</sub>-C<sub>4</sub>)alkyl which may be substituted by an hydroxy or one or several fluorine atoms ; a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl ; or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl.

49. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID N°:3):



in which A7 is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms.

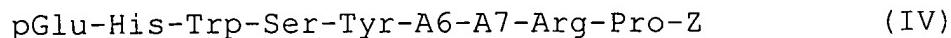
50. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID N°: 4):



in which:

- A3 and A5 are each independently Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, 1Nal, Bal, Pal, 4Pal, or pClPhe ;
- A6 is (S)-spirolactam-Pro ; Gly; D-Pro ; D-Ser(OBu<sup>t</sup>) ; D-Asp(OBu<sup>t</sup>) ; D-Glu(OBu<sup>t</sup>) ; D-Thr(OBu<sup>t</sup>) ; D-Cys(OBu<sup>t</sup>) ; D-His or D-His(Bzl) ; D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg or D-Cha ; D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-1Nal, D-Bal, D-Pal, D-4Pal, or D-pClPhe; D-cyclohexadienyl-Gly ; D-perhydronaphtyl-Ala ; D-perhydrodiphenyl-Ala ; or D-APhe optionally substituted by an aminotriazolyl group ;
- A7 is Leu, Npg or Cha, which may be N-alpha-substituted by a methyl group;
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

51. (previously presented): The method according to claim 48 wherein said peptide analogue has the formula (SEQ ID N°: 5):



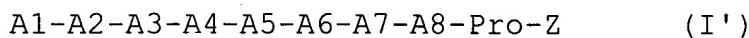
in which:

- A6 is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal, D-Phe, D-

Ser(OBut<sup>t</sup>) or D-Trp;  
- A7 is Leu, MeLeu, Npg or MeNpg;  
- Z is GlyNH<sub>2</sub> ; azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>.

52. (previously presented): The method according to claim 48 wherein the peptide analogue is selected from the group consisting of leuprorelin, [Npg<sup>7</sup>]-leuprorelin, triptorelin, [Npg<sup>7</sup>]-triptorelin, goserelin, [Npg<sup>7</sup>]-goserelin, buserelin and [Npg<sup>7</sup>]-buserelin.

53. (withdrawn): The method according to claim 47 wherein said peptide analogue has the formula (SEQ ID N° : 6) :



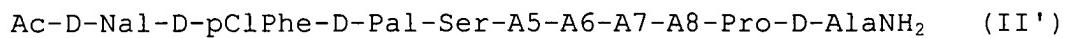
in which:

- A1 is pGlu ; D-pGlu ; Sar ; AcSar ; Pro or a derivative thereof ; Ser ; D-Ser ; Ac-D-Ser ; Thr ; D-Thr ; Ac-D-Thr ; or an aromatic D-amino acid which may be acylated;
- A2 is a direct bond or an aromatic D-amino acid;
- A3 is an aromatic L- or D-amino acid;
- A4 is Ala, Ser, D-Ser, MeSer, Ser(OBut<sup>t</sup>), Ser(OBzl) or Thr;
- A5 is an aromatic L-amino acid or a basic L- or D-amino acid;
- A6 is Gly ; D-Pro ; D-Ser ; D-Thr ; D-Cys ; D-Met ; D-Asn ; D-Pen ; D-(S-Me)Pen ; D-(S-Et)Pen ; D-Ser(OBut<sup>t</sup>) ; D-Asp(OBut<sup>t</sup>) ; D-Glu(O-But<sup>t</sup>) ; D-Thr(O-But<sup>t</sup>) ; D-Cys(O-But<sup>t</sup>) ; D-Ser(O-R<sub>1</sub>) where R<sub>1</sub> is a sugar moiety ; an aliphatic D-amino acid with a (C<sub>1</sub>-C<sub>8</sub>)alkyl or a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl side chain ; an aromatic D-amino acid ; D-cyclohexadienyl-Gly ; D-perhydronaphthyl-Ala ; D-perhydrodiphenyl-Ala ; or a basic L- or D-amino acid;
- A7 is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a

(C<sub>1</sub>-C<sub>4</sub>)alkyl group optionally substituted by one or several fluorine atoms;

- A8 is a basic L- or D-amino acid;
- Z is GlyNH<sub>2</sub> or D-AlaNH<sub>2</sub>.

54. (withdrawn): The method according to claim 53 wherein the peptide analogue has the formula (SEQ ID N° : 7):



in which :

- A5 is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys;
- A6 is (S)spirolactam-Pro, D-Arg, D-NicLys, D-IprLys, D-Cit, D-HCit or D-Asn;
- A7 is Leu, MeLeu, Npg or MeNpg;
- A8 is Arg, NicLys or IprLys.

55. (withdrawn): The method according to claim 53 wherein the peptide analogue is selected from the group consisting of antide, [Npg<sup>7</sup>]-antide, cetrorelix, [Npg<sup>7</sup>]-cetrorelix, abarelix and [Npg<sup>7</sup>]-abarelix.

56. (withdrawn): The method according to claim 47 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

57. (withdrawn): The method according to claim 56 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

58. (previously presented): The method according to claim

47 for the treatment or prevention of breast cancer.

59. (previously presented): The method according to claim 58 which further comprises the sequential, parallel or over a period of time administration of at least one compound selected from the group consisting of an antiestrogen, an aromatase inhibitor and a C<sub>17-20</sub> lyase inhibitor.

60. (previously presented): The method according to claim 47 for the treatment or prevention of prostate cancer or benign prostatic hypertrophy.

61. (previously presented): The method according to claim 60 which further comprises the sequential, parallel or over a period of time administration of at least one compound selected from the group consisting of an antiandrogen, a 5α-reductase inhibitor and a C<sub>17-20</sub> lyase inhibitor.

62. (previously presented): The method according to claim 47 wherein the peptide analogue is delivered to the gastrointestinal tract of the patient.

63. (previously presented): The pharmaceutical composition according to claim 28 wherein the α-cyclodextrin derivative is selected from the group consisting of methylated α-cyclodextrin, hexakis(2,3,6-tri-O-methyl)-α-cyclodextrin, carboxy-methylated α-cyclodextrin and phosphated α-cyclodextrin.

64. (previously presented): The pharmaceutical composition according to claim 28 comprising α-cyclodextrin or

hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

65. (previously presented): The pharmaceutical composition according to claim 64 wherein the peptide analogue is leuprorelin.

66. (previously presented): The pharmaceutical composition according to claim 64 wherein the peptide analogue is [Npg<sup>7</sup>]-leuprorelin.

67. (previously presented): The method according to claim 41 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

68. (previously presented): The method according to claim 67 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

69. (previously presented): The method according to claim 35, which comprises orally administering a therapeutically effective amount of leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

70. (previously presented): The method according to claim 35, which comprises orally administering a therapeutically effective amount of [Npg<sup>7</sup>]-leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

71. (previously presented): The method according to claim 52 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

72. (previously presented): The method according to claim 71 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

73. (previously presented): The method according to claim 47, which comprises orally administering a therapeutically effective amount of leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

74. (previously presented): The method according to claim 47, which comprises orally administering a therapeutically effective amount of [Npg<sup>7</sup>]-leuprorelin in combination with  $\alpha$ -cyclodextrin or hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

75. (previously presented): The method according to claim 62 wherein the  $\alpha$ -cyclodextrin derivative is selected from the group consisting of methylated  $\alpha$ -cyclodextrin, hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin, carboxymethylated  $\alpha$ -cyclodextrin and phosphated  $\alpha$ -cyclodextrin.

76. (previously presented): The method according to claim 71 wherein the  $\alpha$ -cyclodextrin derivative is hexakis(2,3,6-tri-O-methyl)- $\alpha$ -cyclodextrin.

77. (previously presented): The method according to claim 76 wherein the peptide analogue is leuprorelin.

78. (previously presented): The method according to claim 76 wherein the peptide analogue is [Npg<sup>7</sup>]-leuprorelin.

LAW OFFICES  
DENNISON, SCHULTZ, DOUGHERTY & MACDONALD  
SUITE 105  
1727 KING STREET  
ALEXANDRIA, VIRGINIA 22314-2700  
703 837-9600